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The *cis-AB01* Allele Originated From the *A105* Allele, and not From the *A102* Allele

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Researchers in the field of transfusion medicine have a growing interest in the *cis*-AB blood group, which is characterized by a paradoxical inheritance of the *ABO* blood group [1]. The *cis*-AB blood group arises from a glycosyltransferase capable of synthesizing both A and B antigens simultaneously [2]. In addition, affected individuals display more than one phenotype depending on their partnering alleles. *Cis*-AB may eventually lead to *ABO* discrepancy [3]. The *cis*-AB allele was the most common *ABO* subgroup in Korean blood donors [4], and Cho *et al*. [5] found that the *cis*-AB allele was also the most common cause of *ABO* discrepancy in Koreans. From similar contexts, many authors have performed genetic analysis of *cis*-AB with sequencing methods for *ABO* genotyping. These studies have suggested that the *cis-AB01* allele arises from a single polymorphism, 803G>C, in exon 7 of the *A102* allele [6, 7]. However, the sequencing was solely focused on exons 6 and 7. According to a previous study, analysis of intron sequences indicated that individuals with the *A102* allele may be re-classified into those with the *A105* allele [8]. We therefore performed an extended analysis of the genomic sequences of the *cis-AB01* allele, previously known as the *A102* allele, to clarify its genetic background.

Here, we screened five samples of the *cis-AB01* allele through direct sequencing of exons 6 and 7 from samples submitted for *ABO* genotyping between January 2009 and December 2011 to Chonnam National University Hospital and Chonnam National University Hwasun Hospital. We performed *ABO* genotyping for all exons and introns except intron 1 and then compared the *cis-AB01* and *A101* allele sequences. This analysis showed identical point mutations in the *cis-AB01*, compared to *A101* alleles (1142C>T in intron 4, 163T>C and 179C>T in intron 6, 467C>T and 803G>C in exon 7). We found only one nucleotide difference between the *cis-AB01* allele and the *A105* allele, 803G>C, in contrast to the three nucleotides that differed between the *cis-AB01* and *A102* alleles. Based on the prevailing hypothesis that mutations in the *ABO* gene render it capable of synthesizing both A and B antigens, our data led to the speculation that the *A105* allele might have acquired a single point mutation at 803G>C in exon 7 and got converted to the *cis-AB01* allele (Fig. 1). We found that the frequencies of the *A101*, *A102*, *A105*, *O01*, and *O02* alleles were 3.3%, 33.3%, 23.3%, 20.0%, and 20.0%, respectively, in specimens (n=15) collected from individuals with the normal A phenotype. Thus, although *A105* allele is the second most prevalent among *A* alleles, we assume that, without analysis of intron 6 sequences, the *A105* allele can be mistaken

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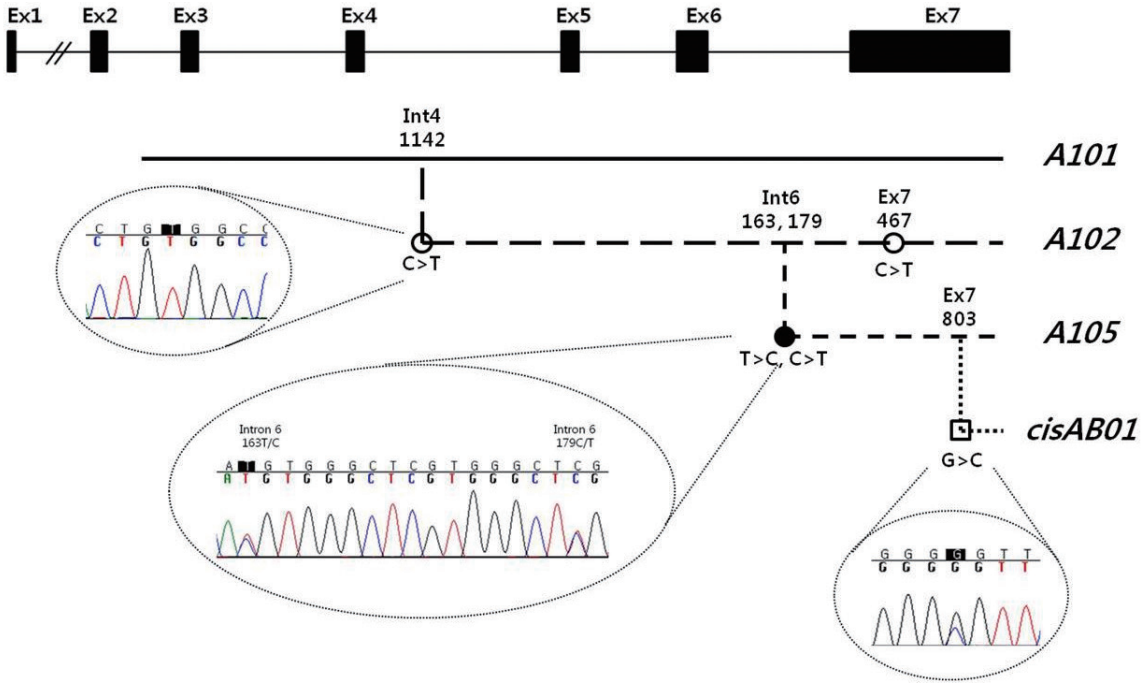

Fig. 1. The molecular origin of the *cis-AB01* allele is the *A105* allele, but not the *A102* allele. The *cis-AB01* allele has five point mutations compared to the *A101* allele as follows: 1142C>T in intron 4, 163T>C and 179C>T in intron 6, 467C>T and 803G>C in exon 7. The *cis-AB01* allele has the only one nucleotide difference of 803G>C compared with the *A105* allele.
Abbreviations: Ex, exon; Int, intron.

for the *A102* allele. Genetic analysis of exons 6 and 7 has been commonly used for demonstrating a new allele [6, 7, 9]; however, our results indicate that further studies are warranted to analyze lineage-specific variations in intron sequences, intron 6 in particular, which is essential for obtaining accurate results of the *ABO* genotyping. Moreover, we suggest performing intron analysis for the *A105* allele in individuals from Southwestern Korea and Japan, both of which are predominant regions of the *cis*-AB allele.

To the best of our knowledge, we have revealed the first complete genome sequence (except intron 1) of the *cis-AB01* allele and shown that it arose from the *A105* allele rather than the *A102* allele. Our results are of significance in clarifying the phylogenetic and epidemiologic characteristics of the *cis-AB01* allele.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Yamaguchi H. A review of cis-AB Blood. Jpn J Human Genet 1973; 18:1-9.
2. Yazer MH, Olsson ML, Palcic MM. The cis-AB blood group phenotype: fundamental lessons in glycobiology. Transfus Med Rev 2006;20:207-17.
3. Cho D, Kee SJ, Shin JH, Suh SP, Ryang DW. Unusual phenotype of cis-AB. Vox Sang 2003;84:336-7.
4. Cho D, Kim SH, Jeon MJ, Choi KL, Kee SJ, Shin MG, et al. The serological and genetic basis of the cis-AB blood group in Korea. Vox Sang 2004;87:41-3.
5. Cho D, Lee JS, Park JY, Jeon MJ, Song JW, Kim SH, et al. Resolution of ABO discrepancies by ABO genotyping. Korean J Lab Med 2006;26: 107-13.
6. Yip SP. Sequence variation at the human ABO locus. Ann Hum Genet 2002;66:1-27.
7. Yamamoto F, McNeill PD, Kominato Y, Yamamoto M, Hakomori S, Ishimoto S, et al. Molecular genetic analysis of the ABO blood group system: 2. cis-AB alleles. Vox Sang 1993;64:120-3.
8. Won EJ, Park G, Cho D, Lim AH, Kwon SY, Song HR, et al. Complete sequencing of the ABO alleles of the common ABO group and rare ABO subgroups in Koreans. Korean J Blood Transfus 2012;23:1-12.
9. Tzeng CH, Chen YJ, Lyou JY, Chen PS, Liu HM, Hu HY, et al. A novel cis-AB allele derived from a unique 796C>A mutation in exon 7 of ABO gene. Transfusion 2005;45:50-5.

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